

In the claims:

Please amend the claims as indicated below. This version of the pending claims will replace all prior versions.

1. (Previously presented) A method of inhibiting secretion from a non-neuronal inflammatory cell comprising administering an agent comprising at least first and second domains, wherein the first domain cleaves one or more proteins essential to exocytosis and the second domain translocates the first domain into the inflammatory cell.
2. (Currently Amended) ~~A~~ The method according to Claim 1, for treatment of disease caused, exacerbated or maintained by secretion from said non-neuronal inflammatory cell.
3. (Currently Amended) ~~A~~ The method according to Claim 1, wherein the agent further comprises a third domain for targeting the agent to said non-neuronal inflammatory cell.
- 4.-7. (canceled)
8. (Currently Amended) ~~A~~ The method according to Claim 3 wherein the third domain comprises a ligand selected from (i) for mast cells, complement receptors in general, including C4 domain of the Fc IgE, and antibodies/ligands to the C3a/C4a-R complement receptor; (ii) for eosinophils, antibodies/ligands to the C3a/C4a-R complement receptor, anti VLA-4 monoclonal antibody, anti-IL5 receptor, antigens or antibodies reactive toward CR4 complement receptor; (iii) for macrophages and monocytes, macrophage stimulating factor, (iv) for macrophages, monocytes and neutrophils, bacterial LPS and yeast B-glucans which bind to CR3, (v) for neutrophils, antibody to OX42, an antigen associated with the iC3b complement receptor, or IL8; (vi) for fibroblasts, mannose 6-phosphate/insulin-like growth factor-beta (M6P/IGF-II) receptor and PA2.26, antibody to a cell-surface receptor for active fibroblasts in mice.
9. (Currently Amended) ~~A~~ The method according to Claim 2 for the treatment of a disease selected from the group consisting of allergies (~~seasonal allergic rhinitis (hay fever), allergic conjunctivitis, vasomotor rhinitis and food allergy~~), eosinophilia, asthma, rheumatoid arthritis, systemic lupus erythematosus, discoid lupus erythematosus, ulcerative colitis, Crohn's disease, haemorrhoids, pruritus, glomerulonephritis, hepatitis, pancreatitis, gastritis, vasculitis, myocarditis, psoriasis, eczema, chronic radiation-induced fibrosis, lung scarring and other fibrotic disorders.
- 10.-21. (canceled)

22. (Currently Amended) ~~A~~ The method according to Claim 1, wherein the agent comprises a first domain that cleaves a protein selected from SNAP-25, synaptobrevin and syntaxin.
23. (Currently Amended) ~~A~~ The method according to Claim 22 wherein the first domain comprises a light chain of a clostridial neurotoxin, or a fragment, variant or derivative thereof which inhibits exocytosis.
24. (Currently Amended) ~~A~~ The method according to Claim 1, wherein the second domain comprises a H_N region of a clostridial polypeptide, or a fragment, variant or derivative thereof that translocates the exocytosis inhibiting activity of the first domain into the inflammatory cell.
25. (Currently Amended) ~~A~~ The method according to Claim 1 for inhibition of constitutive and regulated release from non-neuronal inflammatory cells.
26. (Currently Amended) An agent for inhibiting secretion from a non-neuronal inflammatory cell, comprising at least first, second and third domains, wherein the first domain cleaves one or more proteins essential to exocytosis, the second domain translocates the first domain into the cell, and the third domain binds to said non-neuronal inflammatory cell, wherein said third domain does not substantially bind to neuronal cells.
27. (Currently Amended) ~~An~~ The agent according to Claim 26, wherein the third domain is as defined in Claim 4 targets the agent to an endocrine cell.
28. (Currently Amended) A pharmaceutical composition comprising ~~an~~ the agent according to Claim 26 in combination with a pharmaceutically acceptable carrier.
- 29.- 30. (canceled)
31. (Previously presented) A nucleic acid construct encoding an agent according to Claim 26, said construct comprising nucleic acid sequences encoding the first, second and third domains.
32. (Previously presented) A nucleic acid construct according to Claim 31, operably linked to promoter and terminator sequences, and optionally regulatory sequences, said promoter, terminator and regulatory sequences being functional in a non-neuronal inflammatory target cell to effect expression of said agent in said target cell.
33. (Previously presented) An agent for use in gene therapy, comprising a nucleic acid sequence encoding a first domain which cleaves one or more proteins essential to exocytosis, and a second domain associated with the nucleic acid sequence which, following administration to a patient, translocates the nucleic acid sequence into a non-neuronal inflammatory target cell and, when in said non-neuronal inflammatory target cell, expression of the nucleic acid sequence is effected therein.

34. (Previously presented) An agent according to Claim 33, wherein the nucleic acid sequence is operably linked to promoter and terminator sequences, and optionally regulatory sequences, said promoter, terminator and regulatory sequences being functional in the non-neuronal inflammatory target cell to effect expression of said agent in said non-neuronal inflammatory target cell.

35. (Previously presented) An agent according to Claim 33, wherein the agent further comprises a third domain for targeting the agent to said non-neuronal inflammatory cell.

36. (Previously presented) A method of treating by gene therapy a disease caused, exacerbated or maintained by secretion from a non-neuronal inflammatory cell, said method comprising administering to a patient an agent according to Claim 33.

37. (canceled)

38. (Currently Amended) A method of treating a disease caused, exacerbated or maintained by secretion from a non-neuronal inflammatory cell, said method comprising administering to a patient a polypeptide that cleaves one or more proteins essential to exocytosis, ~~or a nucleic acid encoding said polypeptide, to a patient.~~

39. (canceled)

40. (New) A method of inhibiting secretion from a non-neuronal inflammatory cell, comprising administering an agent comprising at least first, second and third domains, wherein the first domain cleaves one or more proteins essential to exocytosis, the second domain translocates the first domain into the inflammatory cell, and the third domain targets the agent to said non-neuronal inflammatory cell.

41. (New) A method of inhibiting secretion from a non-neuronal inflammatory cell, comprising administering an agent comprising at least first and second domains, wherein the first domain comprises a light chain of a clostridial neurotoxin or a fragment thereof, said light chain or fragment having protease activity that cleaves one or more proteins essential to exocytosis, and wherein the second domain translocates the first domain into the inflammatory cell.

42. (New) A method of inhibiting secretion from a non-neuronal inflammatory cell, comprising administering an agent comprising at least first and second domains, wherein the first domain comprises a light chain of a clostridial neurotoxin or a fragment thereof, said light chain or fragment having protease activity that cleaves one or more proteins essential to exocytosis, and wherein the second domain comprises a H_N domain of a clostridial polypeptide, or a fragment thereof that translocates the first domain into the inflammatory cell.

43. (New) An agent for inhibiting secretion from a non-neuronal inflammatory cell,

comprising at least first, second and third domains, wherein the first domain comprises a light chain of a clostridial neurotoxin or a fragment thereof, said light chain or fragment having protease activity that cleaves one or more proteins essential to exocytosis, the second domain translocates the first domain into said non-neuronal inflammatory cell, and the third domain binds to said non-neuronal inflammatory cell, wherein said third domain does not substantially bind to neuronal cells.

44. (New) An agent for inhibiting secretion from a non-neuronal inflammatory cell, comprising at least first, second and third domains, wherein the first domain comprises a light chain of a clostridial neurotoxin or a fragment thereof, said light chain or fragment having protease activity that cleaves one or more proteins essential to exocytosis, the second domain comprises a H_N domain of a clostridial polypeptide, or a fragment thereof that translocates the first domain into the inflammatory cell, and the third domain binds to said non-neuronal inflammatory cell, wherein said third domain does not substantially bind to neuronal cells.

45. (New) The method of claim 9, wherein the allergies are selected from the group consisting of seasonal allergic rhinitis, allergic conjunctivitis, vasomotor rhinitis and food allergy.